

## ABSTRACT

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Title of diploma thesis: Synthesis and biological evaluation of purine inhibitors of phosphatidylinositol 3-kinases and related protein kinases I.

Cancer is a group of diseases characterized by the uncontrolled, abnormal growth of cells. Anticancer chemotherapy is one of the basic methods for treatment, but its mechanism of action is not specific and targets rapidly dividing cells, including cancer cells as well as certain normal tissues. In recent years one of the most studied ways to improve cancer treatment is inhibition of DNA repair mechanisms. This process can lead to potentially higher efficacy of cytotoxic therapy and thus lower doses of cytostatic agents with benefit of less adverse side effects for the patient. Suitable candidate for this purpose is family of phosphatidylinositol 3-kinase-related protein kinases (PIKK).

In this diploma thesis, sixteen purine analogs of nonselective inhibitor PIKK LY294002 were prepared. We also analyzed chemo-sensitizing properties of these newly synthesized inhibitors in combination with a chemotherapeutic agent doxorubicin in 9 human cancerous and 1 non-cancerous cell lines. Two inhibitors have chemo-sensitizing effect on most cancer cell lines and may have therapeutic potential for the treatment of patient with cancer.